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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/721,118
Filing Date: November 25, 2003
Appellant(s): HWANG ET AL.

JOHN FREEMAN
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 1, 2010 appealing from the Office action mailed on June 11, 2010.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1, 2, 4-46 are pending in the application.

Claims 1, 2, 4, 29-45 are rejected.

Claims 8 and 27¹ are objected to.

Claims 5-7, 9-26 and 46 are withdrawn from consideration.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

¹ The species of claim 8 and 27 have been examined and are considered allowable over prior arts.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS."

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner:

Rejection of claims 1, 4, 27, 29-45 under 35 U.S.C. § 103 (a) as being unpatentable over Needleman et al. (US 2003/0220374 A1) in view of Rosenfield (US 6004751).

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

2004/0052760 A1 MICHELET ET AL. 03-2004

Midorikawa, T. et al., "Hair Growing Composition", JP2003-155218, May 27, 2003, English abstract.

Midorikawa, T. et al. "Hair Growing Composition", JP 2003-155218, May 27, 2003, machine translation, printed on February 8, 2011.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 29-45 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific PGD2 and analog compounds disclosed in the working examples, does not reasonably provide enablement for the entire genus of prostaglandin DP receptor agonists.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Evaluating enablement requires determining whether any undue experimentation is necessary for a skilled artisan to determine how to make and/or use the claimed invention. Factors to be considered in determining whether any necessary experimentation is "undue" include, but are not limited to: a) the breadth of the claims; b) the nature of the invention; c) the state of the prior art, the level of one of ordinary skill; d) the level of predictability in the art; e) the amount of direction provided by the inventor; f) the existence of working examples; and g) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See In re Wands, 858 F.2d 731, 737, 8 U.S.P.Q. 2d 1400, 1404 (Fed. Cir. 1988).

The breath of the claims

Claim 1 is representative of the instant invention and directed to a method of reducing mammalian hair growth by selecting an area of skin including hair follicles from which reduced hair growth is desired, and applying to the said area of skin a dermatologically acceptable composition comprising **an agonist of prostaglandin DP-receptor** in an amount effective to reduce hair growth. Claim 43 is directed to an analogous method which uses a compound selected from **prostaglandin D₂, analogs of prostaglandin D₂, PGJ₂ or an analog of PGJ₂**. Claim 44 is directed to an analogous method which uses **a compound that activates DP receptor signal transduction pathway**. Claim 45 is directed to an analogous method which uses **a compound that inactivates prostaglandin D₂ metabolic pathway**.

The inventions of claims 1 and 44 use the entire genus of the agonists of PGD receptor, which include PGD₂ analogs, derivatives, PGD₂ metabolites and their analogs. See appellant's spec. p. 4, lines 15 – 16.

The nature of the invention

The present invention is directed to a method of controlling unwanted hair growth by locally administering the entire genus of the agonists of PGD receptor, which include PGD₂ analogs and PGD₂ metabolites and their analogs.

The state of the prior art

Agonists of prostaglandin DP receptors were known in the art, as admitted by appellant in specification p. 4, lines 15 -24; Table 1. Prostaglandin D₂ analogs and

derivatives, its sequential metabolites and their analogs also were known at the time of the present invention.

However, prior arts also teach that some of the agonists of prostaglandin DP receptors disclosed by appellant (e.g., BW245C and BW246C) have been used in a hair **growth promoting** agent. See Michelet et al. (US 2004/0052760 A1) [0164], assigned to the same assignee of the present invention². According to appellant's own disclosure, BW245C and BW246C are PGD₂ analogs. See spec. p. 4, Table I, lines 4-5. Midorikawa (JP 2003-155218 A, abstract) also teaches prostaglandins D and derivatives thereof are used in a hair **growing** composition.

The level of predictability in the art

Since the prior utility of prostaglandin DP receptors was known to induce the opposite effect of the present invention, the efficacy of the all of the compounds encompassed by the present invention would have been highly unpredictable to a person of ordinary skill in this art.

The amount of direction provided by the inventor

The present specification discloses examples of PGD₂ analogs, but suggests **any** of the known agonist of prostaglandin DP receptor would be suitable for the purpose of practicing the present invention.

The existence of working examples

Specification pages 11-13 show in vitro human hair follicle growth assay using seven compounds that are PGD₂ or its analogs (i.e., PGD₂, 15-deoxy- delta^{12, 14}-PGD₂,

16,16-dimethyl PGD₂, 15(S)-15 methyl PGD₂, 17-phenyl trinor PGD₂, 11-deoxy-11-methylene PGD₂, 15(R)-15-methyl PGD₂).

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Since the prior art suggests not all agonists of prostaglandin DP receptor are effective for reducing hair growth, and in fact have been used for growing hair, it would be inevitable for a skilled artisan to undergo undue experimentation to test the efficacy of the prostaglandin DP receptors which are not disclosed in the working examples of the appellant's specification.

In conclusion, since prior arts teaches prostaglandin D and at least some of PGD₂ analogs have been used for hair growing agents, appellant's claim that all PGD receptor agonists and PGD₂ analogs are useful for hair growth reduction directly conflicts with what was known to a person of ordinary skill in the art at the time of the present invention. Therefore, undue experimentation is necessary to test the efficacy of prostaglandin DP receptors or compounds that activates DP receptor signal transmission pathway which have not been tested according to the appellant's disclosure. Appellant's specification enables only those PGD₂ and the analogs in the working examples and fails to enable the full scope of the present claims.

(10) Response to Argument

Examiner asserts that appellant's disclosure does not enable the full scope of the method of using the claimed genus of prostaglandin DP-receptor agonists to reduce hair

² Examiner's comment regarding the assignment of the prior art is in error. As appellant has correctly

growth in mammals. Appellant's main argument focuses on assessment of Michelet in the present scope of enablement rejection. In fact, appellant portrays Michelet as "the key to the rejection and the only finding under the heading for the "state-of -the-art"". See Brief, p. 14, first paragraph.

Appellant's statements here are false because Midorikawa was also considered in reaching the conclusion of lack of scope of enablement. The reference, as discussed in the rejection above, teaches that prostaglandin Ds and its derivatives are used as active agents in a hair growth composition for human use. No rebuttal argument has been made regarding Midorikawa in the appeal brief. Secondly, Michelet reasonably suggests to a person of ordinary skill in the art that certain PGD₂ agonists would be inoperable in the claimed hair growth reduction method, rendering the full scope of the present invention highly unpredictable.

1) Midorikawa suggests inoperability and unpredictability of the full scope of the present invention.

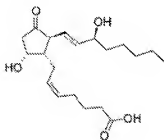
Although Midorikawa has not been discussed in the appeal brief, this reference must be considered to assess the level of state of art and the degree of unpredictability in the art.

As disclosed by appellant in specification, p. 10, prostaglandins contain a cyclopentane ring with the two-side chains alpha (-) and omega (-). Prostaglandins are classified into prostaglandin types A through I based on modifications of the

cyclopentane ring. However, the only naturally occurring prostaglandins are types D through I.

The teaching of Midorikawa is crucial because the reference discloses that Prostaglandins D and its derivatives are the active ingredients in a hair growing composition and suitable for a long-term use.

Prostaglandin D₂ is one of the Prostaglandin Ds and has a structure:



The method of instant claims 1 and 44 use an agonist of prostaglandin DP-receptor. Appellant states in specification "[e]xamples of agonists of prostaglandin DP-receptor include prostaglandin D₂ analogs and prostaglandin D₂-sequential metabolites and their analogs". (emphasis inserted) See spec. p. 4, lines 15 – 16.

In view of Midorikawa's disclosure that prostaglandins D and derivatives, which include prostaglandin D₂, are known as active agents in a hair growing composition, accuracy of appellant's statement that all agonists of DP receptors reduce hair growth is in doubt.

2) Michelet suggests inoperability and unpredictability of the full scope of the present invention.

Appellant argues that the Michelet invention is directed to a method of promoting hair growth with inhibitors of 15-hydroxyprostaglandin dehydrogenase, whose enzyme

activity is not related to appellants DP receptor agonists, BW245C³ and BW246C⁴.

However, the issue here is not whether the disclosed DP receptor agonists are expected to inhibit the specific enzyme or target the specific substrates, PGF₂α or PGE₂. In effort to address this issue, which is irrelevant in determining predictability of the present invention in the art, appellant asserts that Michelet fails to teach the specific means of administration of BW245C or BW246C.

However, the actual issue here should be whether the nature of the present invention is known and state of prior art is predictable so that the lack of explicit disclosure of in the specification as to how to use these DP receptor agonists in hair growth reduction is enabling. The relevant portion of Michelet is paragraph [164], which teaches that the hair growth promoting composition "will additionally contain" particular agonists of prostaglandin receptors. The reference specifically teaches, "the prostaglandin D₂ receptor such as BW245C ((4S)-(3-[(3R,S)-3-cyclohexyl-3-hydroxypropyl]-2,5-dioxo)-4-imidazolidineheptanoic acid) and BW245C ((4R)-(3-[(3R,S)-3-cyclohexyl-3-hydroxypropyl]-2,5-dioxo)-4-imidazolidine-heptanoic acid), the agonists and their precursors". Such disclosure would have reasonably suggested and inferred to one of skill in the art that the prostaglandin D₂ receptors aid in hair growth, or render hair growth reduction inoperable. This is simply because a reasonable person of chemical art would have incorporated to a hair growth promoting composition only those components that would be advantageous to the intended goal and exclude those that

³ ((4S)-(3-[(3R,S)-3-cyclohexyl-3-hydroxypropyl]-2,5-dioxo)-4-imidazolidineheptanoic acid)

⁴ ((4R)-(3-[(3R,S)-3-cyclohexyl-3-hydroxypropyl]-2,5-dioxo)-4-imidazolidine-heptanoic acid)

are expected to counteract or adversely affect hair growth. Appellant also teaches in the present specification that the hair growth reduction composition of the present invention "may include one or more other types of hair growth reducing agents". See spec. p. 5, line 3.

Thus, appellant's argument that Michelet suggests nothing of the effects of PGD2 receptor agonists on modulation of hair growth is unpersuasive. The prior art reasonably casts doubts on the operability of the presently claimed method of using all prostaglandin D2 agonists.

3) In view of the prior art teaching, the present working examples are insufficient to enable the full scope of the invention.

Given the state of the art, sufficient amount of guidance by the inventor and working examples would have been necessary to render appellant's disclosure enabling for the full scope of the agonists of DP receptors. However, such was not adequately provided in the specification.

The court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), stated:

[I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof.

The court in In re Fisher also held that, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more embodiments may be required. See 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity).

In the present specification, Examples 1-11 are general formulations for topical compositions which do not identify what specific agonists of DP receptor may be used. Nor the actual physiological effects of such compositions in mammals are provided in the specification.

The actual working examples provided in the applications are the in vitro tests of selected agonists of PGD₂, PGJ₂ and their analogs in Table III and IV⁵. None of the examples show efficacy of BW245C and BW246C, the PGD₂ receptor agonists of Michelet, in hair growth reduction.

In response to appellant's remarks regarding the adequacy of in vitro tests, examiner asserts that appellant has a high burden of showing enablement of the claimed class of DP agonists in vivo, particularly in view of Midorikawa which teaches prostaglandins D and derivatives thereof are active hair growing agents used in topical compositions. The class of PGDs and their derivatives overlap with the agonists that are claimed in the present invention (e.g., PGD₂).

In this case, evidence reasonably casts doubts to enablement of the full scope of the present invention. It is not obvious from appellant's disclosure of working examples

⁵ Contrary to appellant's statement in Brief, p. 19, Table IV of specification lists four compounds.

that compounds which have not been tested but have been identified as DP receptor agonists would reduce hair growth in mammals as claimed by appellant.

4) Evaluation of evidence as a whole weighs against finding enablement of the full scope of the invention.

Appellant's statement that using agonists of DP agonists are in "highly developed state of the art in November 2003" is erroneous. Midorikawa teaches that Prostaglandin Ds and derivatives thereof are known as hair growing actives, thus Appellant's claimed method are, at least in part, in direct contrast to the known method of using Prostaglandin Ds and its derivatives to promote hair growth. Michelet also suggests that certain PGD₂ receptors would be inoperable in the claimed method of reducing hair growth. Although agonists of DP agonists have been identified as appellant discloses, whether these compounds are merely known is not a determining factor here. What must be considered is the specific teachings of Midorikawa and Michelet with respect to the effects of prostaglandin Ds and PGD₂ agonists in hair growth modulation. Evidence weighs against enablement of the full scope of the present invention, as hair growth reduction properties of the claimed class of DP agonists in mammals is highly unpredictable in the art.

Appellant also argues that only routine experimentation would require to determine efficacy to test the disclosed DP agonists compounds. Examiner respectfully disagrees. The scope of the present method of using the whole class of agonists of DP receptors extends to further identifying and testing the agonists that are not disclosed in the appellant's specification. Further to respond to appellant's remarks here, testing of

hair growth reduction in mammals would require on-going screening and protocol, as there are intrinsic and extrinsic factors that may affect hair growth, such as aging, diet, and diseases. See Hattori et al., J. of Derm. 1985, vol. 10:45-54, cited by appellant on April 23, 2004. Moreover, the unpredictability of the outcome of the screening by the skilled artisan (as indicated above), would render such experimentation undue.

In conclusion, proof of enablement will be required for non-exemplified members of the claimed genus of agonists of DP receptor in this case. Evidence indicates that at the time of the present invention prostaglandin Ds were known as hair growing active agents and specific PGD₂ were used with hair growing agents. Given such state of prior art, one of ordinary skill in the art could not predict that all DP receptor agonists would reduce hair growth in mammals as claimed by appellant. Examiner thus maintains the position that a person of ordinary skill in the art could not use the claimed genus as a whole without undue experimentation.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/GINA C. YU/

Art Unit: 1617

Primary Examiner, Art Unit 1617

Conferees:

/Fereydoun G Sajjadi/
Supervisory Patent Examiner, Art Unit 1617

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614